REMARKS

Applicants acknowledge that claims 12, 16, 76-78, 81, 86-88, 91, 106, 108, 110, 112 and 115-123 were pending and under examination. Claims 12 and 16 have been canceled. Cancellation of these claims is made without prejudice to further prosecution. Applicants reserve the right to pursue claims to the same or similar subject matter in future applications. Applicants have amended claims 76, 86, 81, 86, 88, 91, 108, 110, 112, 115-117, and 120. Thus, claims 76-78, 81, 86-88, 91, 106, 108, 110, 112 and 115-123 are pending and under examination. No new matter has been added.

Interview

Applicants thank Examiners Wollenberger and McGarry for conducting a personal interview with Applicants' representatives. Issues related to the rejections under 35 USC 112 and 102 as set forth in the Office Action were discussed. Applicants agreed to remove the word pharmaceutical from claims 81, 91 and 120 and to clarify that the double stranded RNA is not two strands that are covalently linked to one another. It was agreed that such amendments should be sufficient to overcome the corresponding rejections. It was agreed that the rejection for a lack of enablement of claims 110, 112 and 115-123 should be withdrawn.

Double Patenting

Claims 12, 16, 76-78, 81, 86-88, 91, 106, and 108 remain provisionally rejected and new claims 115-117 and 119-123 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 7, 8, 13, 14, 20, 25, 27 of copending Application No. 10/255,568.

As discussed in the Interview, it is requested that the provisional rejection be withdrawn and maintained in the later filed case if appropriate.

Claims 12, 16, 76, 78, 86, 88, 106, 108, 110, 112, 115-118 and 120-123 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over new claims 30-49 of copending Application No. 11/142,866.

As discussed in the Interview, it is requested that the provisional rejection be withdrawn and maintained in the later filed case if appropriate.

Claim Rejections – 35 USC § 112

Claims 81 and 91 remain rejected and new claims 115-116 (which depend on 81 or 91), and 120 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Applicants have amended claims 81, 91 and 120 to remove the terms "pharmaceutical" and "pharmaceutically acceptable." It is believed that the amendment is sufficient to overcome the rejection.

Claims 110 and 112 remain rejected and new claims 115-123 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Claims 110 and 112 include the limitation that the isolated RNA includes one or more "non-naturally occurring nucleotides or deoxyribonucleotide or non-standard nucleotide." As discussed in the interview with the Examiners, the use of modified nucleotides or chimeric molecules was well known in the art at the time of the invention. Non-naturally occurring nucleotides are well-known in the art and are routinely used in DNA and RNA based methods. These types of nucleotides have been used in the antisense field for years. For instance US Patent No. 5,594,122 in column 6 lines 18-43 and US Patent No. 5,457,189 in column 10 lines 36-677 describe the use of modification and base analogs in antisense oligonucleotides.

The instant patent application provides a teaching that modified nucleotides (non-naturally occurring nucleotides or deoxyribonucleotide or non-standard nucleotides) can be used in

the RNA of the invention. An assay to examine activity of the isolated RNA molecules of the invention is also described (paragraph spanning pages 5 and 6 and Example 1). Thus, one of skill in the art would not need to undertake undue experimentation to practice the claimed invention.

Claim Rejections – 35 USC § 102

Claims 12, 16, 76-78, 81, 86-88, 91, 106, 108, 110 and 112 remain rejected and new claims 115-123 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al. (WO 94/01550).

As discussed in the interview with the Examiners the claims have been amended to clarify that the separate strands are not covalently linked. It is believed that the amendment to the claim language should be sufficient to distinguish the claimed invention from Agrawal et al.

Claims 12, 16, 76-78, 81, 86-88, 91, 106, 108, 115-117 and 119-123 are rejected under 35 U.S.C. 102(a) as being anticipated by Hammond et al. (2000) *Nature* 404:293-296, as evidenced by Elbashir et al. (2001) *Genes & Development* 15:188-200.

Even if one were to conclude that Hammond et al described a double stranded RNA of 21-23 nucleotides in length based on the teachings of Elbashir et al (which Applicants do not concede) such a teaching would not inherently anticipate the claims because the material does not include an element of the claims. Each of the claims requires that the RNA corresponds to a mammalian cellular mRNA. The RNA in Hammond et al corresponds to a Drosophila mRNA. Thus, Hammond et al does not anticipate any of the pending claims.

Furthermore, each of the pending claims is directed to isolated double stranded RNA of about 21 to about 23 nucleotides. The authors of Hammond et al specifically taught that they could not determine if the RNA was single- or double-stranded (page 295, emphasis added):

> "...Active fractions also contained an RNA species of 25 nucleotides that is homologous to the *cyclin E* target (Fig. 4b, northern). The band observed on northern blots may represent a family of discrete RNAs because it could be detected with probes specific for both the sense and antisense *cyclin E* sequences and with probes derived from distinct segments of the dsRNA (data not shown). At present, we *cannot* determine whether the 25-nucleotide RNA is present in the nuclease complex in a double-stranded or single-stranded form..."

Thus, the teachings of Hammond et al would not have led one of skill in the art to produce a double stranded RNA of about 21 to about 23 nucleotides in length for mediating RNAi.

Although Applicants traverse the rejection, Applicants have also submitted a declaration under 37 CFR 1.131. Hammond et al. was published March 16, 2000, two weeks prior to the filing date of the provisional patent application to which the above-identified patent application claims priority. Attached is a Declaration of prior invention under 37 CFR 1.131, stating the invention was made prior to the publication.

The attached Declaration of Dr. Philip Zamore describes a manuscript that was accepted for publication by the journal Cell prior to the March 16, 2000 publication of Hammond et al. The Cell manuscript (Zamore et al Cell 101, 25-33 (2000)), which was published on March 31, 2000 by the inventors of the above-identified patent application, describes data that was included in the provisional patent application to which the instant patent application claims priority. The data in Zamore et al is sufficient to establish that the teachings asserted by the Examiner to be contained in the Hammond et al publication when it is read in the context of Elbashir et al. was previously invented by the Applicants. When an applicant wishes to overcome a § 102(a) anticipation rejection, "'all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show.'" In re Tanczyn, 347 F.2d 830, 831 (C.C.P.A. 1965), citing In re Stempel, 241 F.2d 755, 759 (C.C.P.A. 1957). Thus it is believed that in addition to the arguments presented above, the rejection should be withdrawn in view of the attached declaration.

Claims 12, 16, 76-78, 81, 86-88, 91, 106, 108, 110, 112, 115-117, and 119-123 are rejected under 35 U.S.C. 102(a) as being anticipated by Hamilton et al., (1999) *Science* 286:95-952.

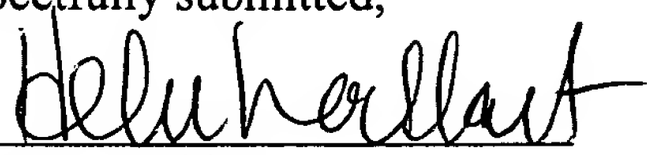
Hamilton et al., does not anticipate the claimed invention because it does not describe a number of elements of the presently rejected claims. For example, Hamilton *et al.* does not disclose an RNA as presently claimed having sequence correspondence to a mammalian cellular mRNA. Each of the pending claims includes the limitation that the RNA corresponds to "mammalian cellular mRNA". Hamilton et al. describes the use of small RNAs for posttranscriptional gene silencing of cellular and viral RNAs in plants. In one experiment Hamilton et al analyzed three tobacco cell lines carrying a GUS transgene. As far as Applicants are aware, the GUS transgene technique is based on expression of beta-glucuronidate gene from the bacterium E. coli, rather than a mammalian gene. Additionally, Applicants note that a claim reciting a mammalian cellular mRNA target is patentably distinct from a claim reciting a viral mRNA target according to the Restriction Requirement dated September 15, 2005. Thus, the pending claims are not anticipated by Hamilton et al.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: November 6, 2006

Respectfully submitted,

By 

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